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13. ABSTRACT *(Maximum 200*

Background. The fluctuating levels of ovarian steroid hormones that characterize the phases of a women's menstrual cycle have metabolic effects that may significantly impact upon the physiologic process of acclimatization to hypobaric hypoxia in military women deployed to high mountain terrain. The state of altitude acclimatization affects physical performance and altitude-related casualties. **Purpose and Scope.** Because no previous information exists, the first year of this three-year study was designed to characterize the effects of menstrual cycle phase on altitude acclimatization in women. The mechanism(s) mediating the effects will be investigated in the subsequent years. **Progress.** The first-year studies were completed in late August 1996. Biochemical and statistical analyses are in progress. **Results and Significance.** Preliminary findings suggest that women have greater effective alveolar ventilation, less plasma volume contraction and greater fat loss with altitude acclimatization during the luteal phase of the menstrual cycle. Although many results are pending, these initial data appear to support the hypothesis that ovarian steroid hormone fluctuations can affect altitude acclimatization. This data may serve as a basis for devising interventions and strategies to maximize the performance and well-being of military women deployed to high mountain environments.

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Lorna J. Moore 10/16/96

PI - Signature Date

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INTRODUCTION

Project purpose and scope. This project is to examine the effect of the menstrual cycle on acclimatization to high altitude (4300 m) in healthy, normally menstruating women. In year one of this three-year project, the period covered in this report, 20 healthy women were studied in the follicular and the luteal phases of the menstrual cycle while residing at sea level and again, in 16 of these women, in either the follicular or the luteal phase of the menstrual cycle during the course of 12 days sojourn in the US Army Research Institute of Environmental Medicine (USARIEM), Maher Memorial Research Laboratory at the summit of Pikes Peak, CO (4300 m).

Studies were conducted to test the hypotheses that 1) fluctuation in ovarian hormones during the menstrual cycle influenced ventilatory, cardiovascular, hematological and metabolic parameters affecting oxygen transport or utilization; and that 2) ventilatory, cardiovascular, hematological and metabolic acclimatization to altitude were enhanced during the luteal compared with the follicular phase of the menstrual cycle. Studies are planned for years two and three to test the general hypothesis that the effects of menstrual cycle phase on acclimatization to high altitude are mediated through interaction with the alpha limb of the sympathetic nervous system.

Project significance. This research will fill major gaps in the understanding of effects of high altitude on the well-being and physical performance of women. Results of this study will provide a rational basis for planning military operations in high mountain terrain that include women service members. Results will assist in identification of effective prophylaxsis and/or treatment of altitude illness, and in devising strategies to minimize performance decrements in military women deployed to strategic high-altitude locations.

Project background. No previous study has systematically evaluated the influence of ovarian hormones on acclimatization to high altitude. Gender differences attributable to ovarian hormone fluctuations are likely for reasons detailed below.

1) *Ovarian hormonal fluctuations of the menstrual cycle.*

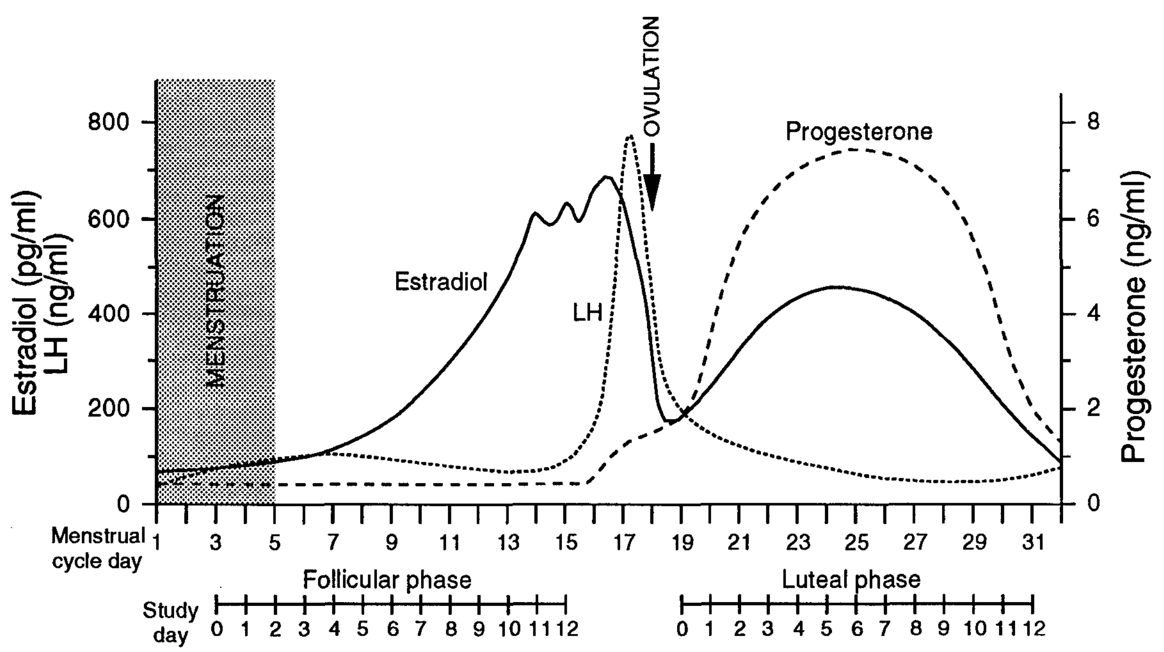


Figure 1: Hormonal concentrations during the menstrual cycle.

2) *Influences of gender and ovarian hormones on ventilation and ventilatory control.* Women have higher levels of resting alveolar ventilation per unit metabolic rate (lower end -tidal or arterial PCO2 values) than men (1,12). This difference appears at the onset of menses and is diminished after the age of menopause, suggesting that ovarian hormones are involved. The increase in ventilation results in part from stimulatory effects of progesterone, as demonstrated by our and other investigators' work showing that the administration of progesterone raises ventilation in men and women, particularly when combined with estrogen (22).

Women, in some but not all studies, have increased hypoxic ventilatory responses when normalized to body size (1). An increase in hypoxic ventilatory drive occurs during the luteal compared with the follicular phase of the menstrual cycle and during pregnancy (22), again suggesting that ovarian hormones are involved.

More direct evidence that gender differences in ventilation involve the actions of ovarian hormones derives from experimental animal and human studies involving exogenous or endogenous elevations in progesterone, and estrogen. Endogenous elevations in these hormones in pregnant cats are accompanied by an increase in ventilation and hypoxic as well as hypercapnic ventilatory sensitivity. The stimulatory effects on hypoxic ventilatory sensitivity occur at the level of the carotid body as demonstrated by an increase in carotid body neural output response to hypoxia when recording from the intact nerve as well as when recording from

the distal (carotid body) end of the cut nerve, indicating that the site of the increased neural activity is the carotid body rather than descending (central) neural stimulation. Exogenous administration of progesterone but not estrogen alone to castrate female cats also raised carotid body neural output responsible to hypoxia (22). When progesterone was combined with estrogen, a greater and more consistent in crease in carotid body neural output response to hypoxia occurred which due to an increase in carotid body neural response and an increase in central neural translation of the carotid body signal into a rise in ventilation (22).

3). Influences of gender and ovarian hormones on cardiovascular and hematological factors. It is well known that women suffer from cardiovascular disease less frequently than men, at least until after the age of the menopause at which time rates in women rise to approximate those of men. The influences of normal, cyclic variation in ovarian hormones during the course of the menstrual cycle have been less thoroughly investigated. In recent, carefully controlled studies carried out within the same woman in the two phases of the menstrual cycle, women in the luteal phase demonstrated a rise in cardiac output, a fall in blood pressure, a slight but not significant increase in blood volume and a rise in circulating catecholamine norepinephrine) levels (Chapman and Zamudio, personal communication). These data suggest that there is peripheral vasodilation in the luteal phase, to which an increase in serum catecholamines may be a compensatory response. There is also a rise in plasma renin activity , an increase in atrial natriuretic factor and an increase in aldosterone. These changes are consistent with peripheral vasodilatation and suggest that salt and water are being retained to maintain vascular pressure.

Hemoglobin concentration is lower in women than men, due probably to inhibitory actions of estradiol and possibly progesterone on erythropoietin production as well as to the volume regulatory influences of ovarian hormones. The coagulation system is also affected by ovarian hormones. There is an increased risk of venous thromboses and pulmonary embolism in the presence of ovarian hormones.

4). Influences of gender and ovarian hormones on metabolic factors. Men and women differ in body composition with women exhibiting a greater proportion of body fat than men. During exercise, women use fat as fuel more than men, especially during the luteal phase of the menstrual cycle. Estradiol-related actions on substrate utilization include a depression of gluconeogenesis and glycolgenolysis, an increased insulin:glucagon ratio and circulating growth hormones. Progesterone also mobilizes free fatty acids and conserve glucose. Thus the hormonal influence present in the luteal phase all favor metabolism of fat over glucose (4,5,13,14,19,24).

BODY

1.)) Preparation (September , 1995 - February, 1996:) Work began during year one (Sept. 22, 1995 - Sept. 21, 1996) in September 1995 in an effort to finalize human volunteer consent forms, and preparations for advertising and screening prospective volunteers. During the course of the fall and winter months, decisions were made as to the amount of various supply items, types of instrumentation and costs of items required for the conduct of the sea level and high altitude phase of testing. By the end of February, more than 100 volunteers had been screened. Twenty-one volunteers consented to participate and of these, twenty completed the sea level series of tests. All women resided in the Palo Alto - San Jose, California area. None were native to altitudes greater than 2500 m and none had been at altitudes > 1500 m for the 6 months prior to the sea level phase of testing. Nearly all the volunteers were undergraduate or graduate students at Stanford University. Dr. Gail Butterfield, co-investigator on this project, was in charge of volunteer recruitment.

The characteristics of the volunteers are shown below.

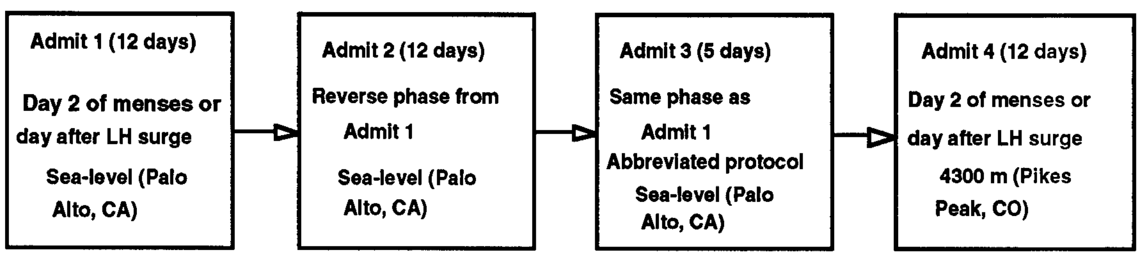
Volunteer characteristics

SL n=20, HA n=16	mean ± SE
Age (yr, range)	22.6 ± 0.8 (19-34)
Height (cm, range)	167 ± 1 (159-175)
Weight (kg, range)	63.4 ± 1.7 (53.6-85.1)
Resting HR (bpm)	66 ± 3
Resting MAP (mmHg)	80 ± 2
VO_2 max (ml/kg/min)	42.8 ± 1.3 (33.2-56.0)

2). Conduct of sea level tests (March - June, 1996): Formal testing of volunteers commenced following final approval of the first year study protocol by the institutional review committees from the University of Colorado, Stanford

University, USARIEM, and the US Army Surgeon General's Human Use Review for Research and Development (HURRAD). Each volunteer underwent extensive studies during three separate time periods, once in both the follicular and the luteal phase of her menstrual cycle and one final time in either the follicular or luteal phase of her cycle. The testing took place with the volunteers residing in a metabolic ward at the Palo Alto VA Medical Center to facilitate dietary control and measurement of metabolic parameters. For that reason, each testing period was designated as an "admission" to the metabolic ward (i.e., Admission #1-3.) To be consistent, each volunteer's 12-day residence at high altitude was designated "Admission 4". The schedule of tests for each woman volunteer during the sea-level phase is shown diagramatically below.

Research Design



- Each woman was her own control for sea-level follicular vs. luteal phases
- Women were measured in either follicular or luteal phase at altitude
- A controlled diet was maintained throughout the studies

The controlled diet was maintained during each of the sea-level admission and during high altitude testing in order to assure that the women were receiving the same proportions of calories from carbohydrates, fats and proteins during each test phase. In addition, diet was adjusted during the first admission to assure that the volunteers were in nitrogen balance.

The testing schedule which each volunteer underwent is shown in appendices A, B and C for admissions #1, 2 and 3. Each "x" designates a day on which the measurements were made. Approximately half the women were in their follicular phase during admission #1 with the remainder in their luteal phase. Follicular phase was detected by the onset of the menses; luteal phase was detected by a positive ovulation predictor test which was based on the detection of the LH surge in twice daily urine samples.

Virtually all the above tests were carried out successfully. Only the "doubly labeled water", α– and β-adrenoreceptor measurements, and venous tone studies described in the original proposal were discontinued for reasons of high cost, blood sample

volume required and the possibility that the substrate utilization studies carried out on day 10 would interfere with the results of the doubly-labeled water tests.

The methods employed were described in the original contract application. To recapitulate briefly, each type of measurement was carried out as follows:

a) Ventilation. Forced vital capacity (VC) was measured in standing volunteers. In seated volunteers, ventilation (VE) was monitored while breathing room. Measured were minute ventilation, breathing frequency, tidal volume, end-tidal PO_2 and PCO_2, arterial O_2 saturation, and heart rate. End-tidal PCO_2 is a measure of alveolar ventilation per unit CO_2 production and is the classic indicator of acclimatization to altitude. The measurement of hypoxic ventilatory response (HVR) was based on a progressive, isocapnic hypoxic test used frequently in our and other's studies.

b) Sympathetic nervous system activation. Sympathetic nervous system activity was assessed by measurement of heart rate (HR) variability, and circulating and urinary catecholamine (catechols) concentrations. Heart rate variability was analyzed by power spectrum analysis during 24-hour Holter monitor recordings in order to determine the relative sympathetic and parasympathetic dominance as previously described (16). Daily 24-hour urinary collections were collected for analysis of catecholamine levels with samples divided between daytime and nocturnal collections. Plasma catecholamine was analyzed in arterial samples obtained from venous samples and, on day 10, from arterial samples using high-performance liquid chromatography as described by Hallman *et al* (15).

c) Hemodynamic studies. Blood pressure was measured from the arterial line and routinely from armcuff sphygmomanometer. Cardiac output during year 1 was measured noninvasively by acetylene rebreathing at rest and during exercise (20). Systemic vascular resistance was calculated from the cardiac output and blood pressure measurements.

d) Blood volume and volume regulatory hormones. Red cell mass was measured using carbon monoxide rebreathing and was used to calculate plasma volume and total blood volume from hematocrit using previously published methods (23,25) on the days indicated. Plasma renin activity, serum aldosterone, plasma atrial natriuretic peptide and ADH were measured from venous samples using radio-immunoassay to monitor volume regulatory hormones (2,17,21). ADH and aldosterone were measured from 24-hr urine collections.

e) Lean body mass. Body composition, *i.e.* the relative proportions of lean and fat tissue were determined by DEXA (dual x-ray absorptiometry) scan.

f) Total body water. During blood volume studies, body water was measured using a deuterium-based technique and extracellular fluid volume was measured using sodium bromide.

g) Resting and exercise O_2 uptake. Resting measurements were made after an at least 4 hour fast in seated volunteers. Exercise measurements were made during

cycle ergometry using conventional techniques for measurement of O_2 uptake, CO_2 production and volume. During exercise, maximum O_2 uptake was defined as the value obtained during progressive cycle exercise (200 kg*m/min every 2 min) where O_2 consumption fails to increase with an increase in workload (23).

h) Basal metabolic rate and dietary control. In order to differentiate fluid loss from loss of body mass, diet was controlled and maintained at a composition approximating 12-14% of calories from protein, 32-40% from fat and the remainder from carbohydrates. Sea level energy requirement was determined by feeding volunteers a standard diet, adjusted over 10 days for changes in body weight. Adequacy of energy intake was validated by determination of N_2 balance, a more sensitive measure of the adequacy of energy intake than body weight (8). Energy intake on day 1 at high altitude was matched to energy requirement at sea level, and adjusted on subsequent days based on changes in basal metabolic rate (BMR), as previously done in men. BMR was determined by indirect calorimetry in the morning before rising every other day at altitude and energy intake was matched to energy need daily. Body weight was monitored daily upon rising and after voiding. Fluid intake was prescribed and monitored.

i) Substrate utilization. Glucose, glycerol and palmitate kinetics were measured at rest and during moderate steady state exercise at 50% of the sea level on admissions #1 and #2 and at approximately 65% of the sea level VO_2max on admission #3. The palmitate was included to monitor both production, utilization and oxidation of FFA. Glucose is included to monitor glucose kinetics. Use of the tracers allowed estimation of rates of appearance, disappearance, and clearance of glucose, glycerol, leucine and palmitate as previously published (6,7). It should be noted that although the use of the stable isotopes was expensive, it avoided the exposure of the volunteers to radioactive substances.

The proposed studies were performed using a mixture or "cocktail" which contained all metabolites. Total body water was measured before the metabolite kinetic studies, as to not influence the isotopic enrichment of deuterium labeled isotopes infused during exercise. Volunteers were studied after a 12-hour fast and 36 hr of limited exercise. A flexible catheter (20 gauge) was inserted in a vein of one arm or hand for the constant infusion of the metabolic cocktail of ^{2}H-glucose (9 μg/kg/min), ^{2}H-glycerol (9.2 μg/kg/min), and ^{13}C-palmitate (5.1 μg/kg/min). The infusion began with a bolus and then at the rate indicated above for 90 min before the start of exercise to ensure equilibrium with body pools. Total dose of fuels for a 60 kg volunteer did not exceed 0.6 gm glucose and 0.11 gm glycerol.

j) Hematologic and coagulation factors. Samples were obtained for measurements of plasma erythropoietin concentration by radio-immunoassay and reticulocyte counts by standard laboratory techniques. Fibrinogen was measured by a quantitative determination of fibrinogen based on the Clauss method (Organon Teknika Fibriquik) (9). Fibrinolytic activity was screened using the euglobulin clot lysis time, ECLT (11). Other fibrinolytic tests included: 1) tissue plasminogen activator (tPA) using Asserachrom tPA, an enzyme immunoassay (Diagnostica Stago/American Bioproducts) and 2) plasminogen activator inhibitor-1 (PAI-1)

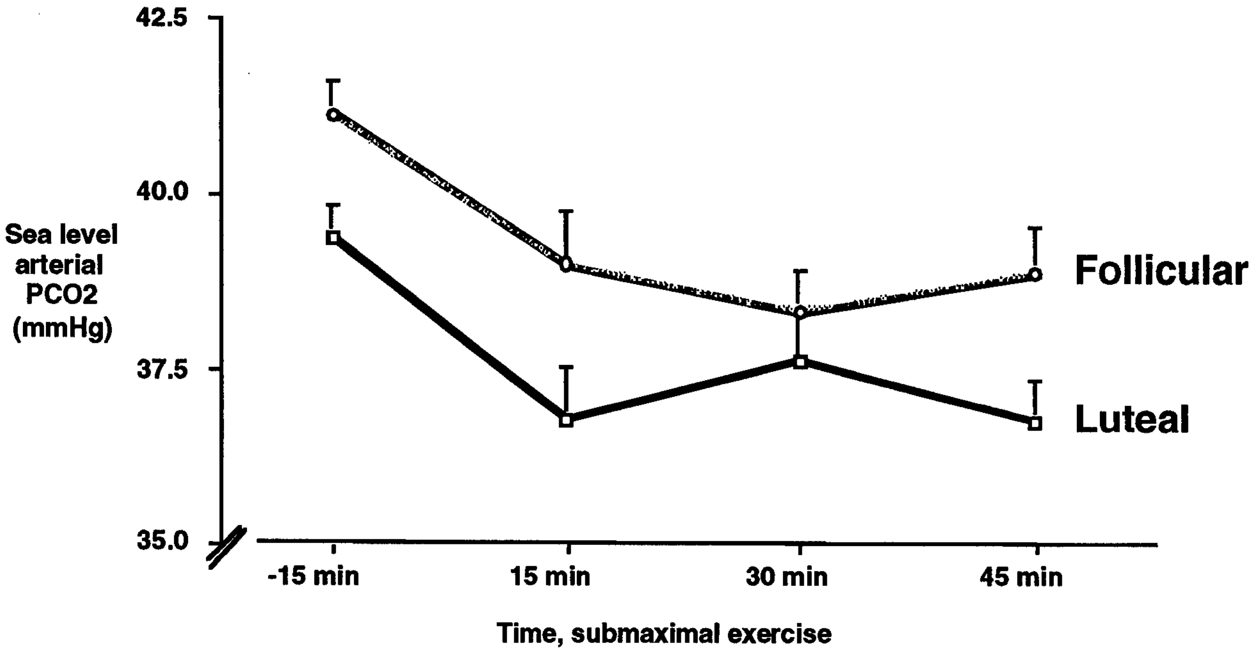
using Stachrom PAI, a quantitative determination of PAI by a synthetic chromogenic substrate method (10). Von Willebrand factor antigen is measured to indicate acute phase activation using Laurell rocket immunoelectrophoresis (18).

k) Ovarian hormones. Estrogen and progesterone levels were measured in 24-hour urine samples and in venous samples drawn periodically (Table 2) in order to quantify hormonal status and menstrual cycle phase using radio-immunoassay (3).

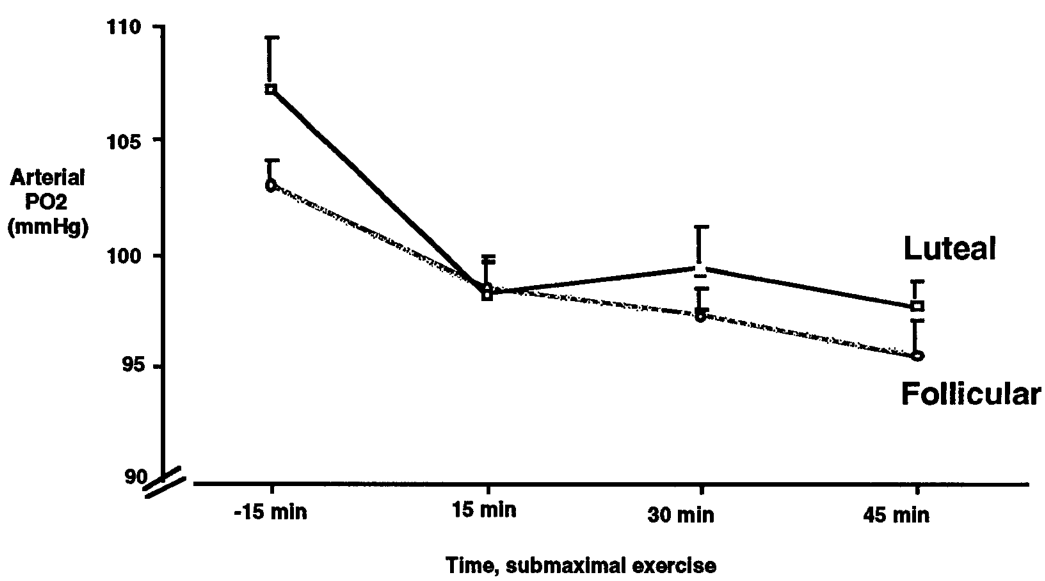
l) Acute Mountain Sickness (AMS). Symptoms of acute mountain sickness were assessed daily using two different validated, self-assessment instruments: the Environmental Symptoms Questionnaire (ESQ) and the Lake Louise AMS Scoring System questionnaire (LLS).

Because the analysis of most of the samples collected awaited until completion of the high-altitude phase of testing which ended in late August, 1996 (see below), comparatively little of the sea level data has been completely analyzed. That information which required minimal processing has been examined. However, these results are only preliminary as the hormone analyses required for confirmation of cycle phase have only been recently completed and results not yet used to decide the composition of the follicular vs luteal phase groups in the sea level studies. Nonetheless, some preliminary findings emerge from the data examined thus far.

As hypothesized, alveolar ventilation was higher (lower arterial PCO_2) in the luteal than the follicular phases of the menstrual cycle. This effect was particularly apparent during exercise as demonstrated by the figures below.



In addition arterial PO2 during exercise at sea level tended to be higher in the luteal than the follicular phase women.



3). Conduct of high-altitude tests (July - August, 1996): Depending on each volunteer's menstrual cycle, schedules were developed and travel arrangements tentatively made to transport each volunteer by air to Colorado Springs, CO at the onset of either her follicular or luteal phase of the menstrual cycle. Assignment to each cycle phase was made essentially at random with consideration being given to

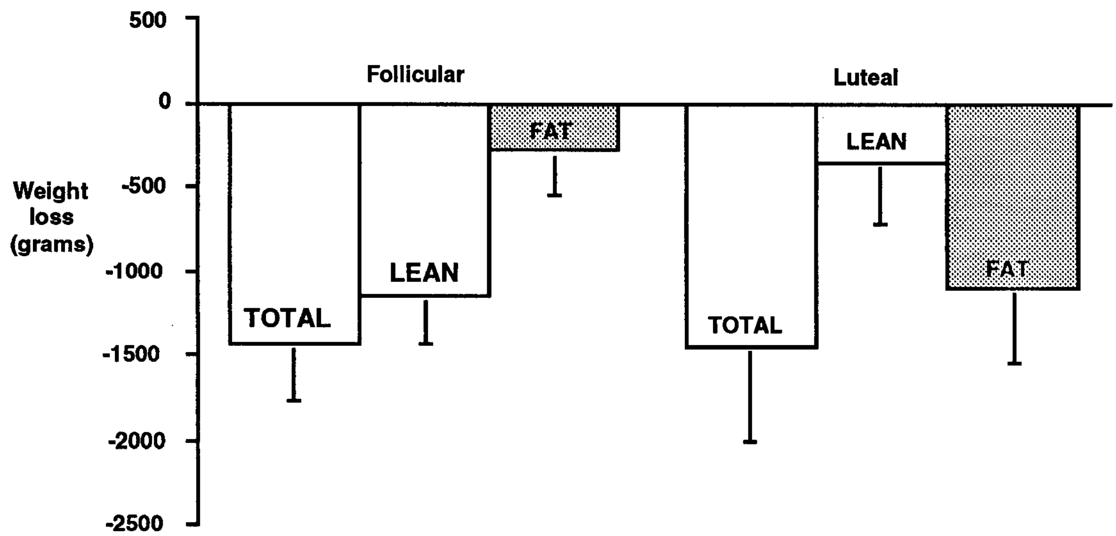
the constraints of the testing schedule for measurements to be carried out on Pikes Peak.

The tests on Pikes Peak were termed "admission #4". The testing schedule which each volunteer underwent is shown in appendix D. Methods employed were the same as those described above.

Since studies were completed in late August, most samples have not yet been fully analyzed. Nonetheless, certain preliminary findings emerge and are portrayed below. As stated above, these findings are preliminary insofar as the hormone based confirmation of cycle phase has not yet been completed.

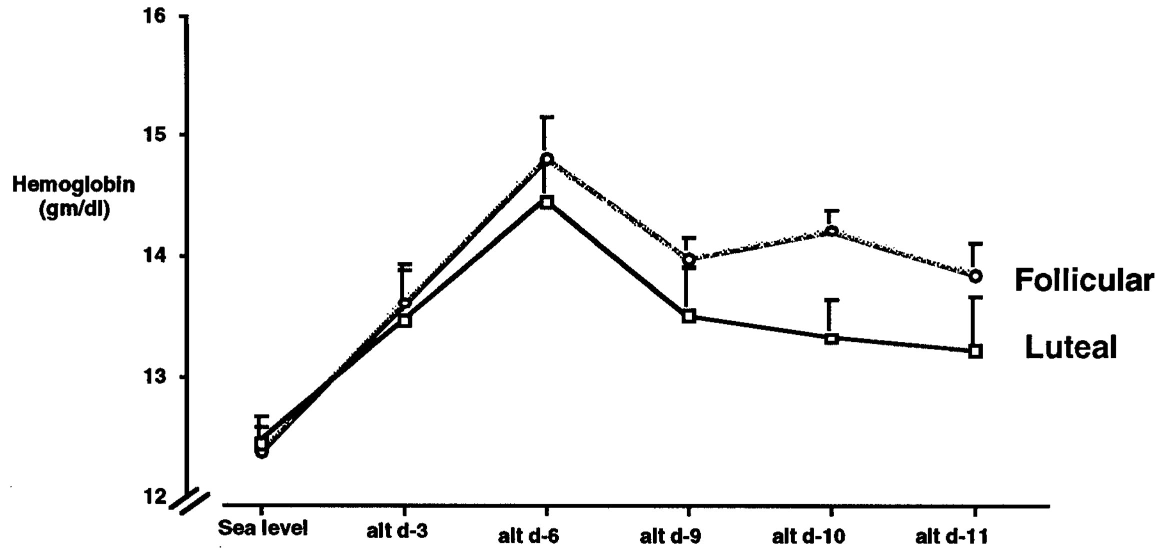
Most of the women lost body weight, the loss of weight averaging 1.5 kg. The weight loss occurred despite increasing daily caloric intakes in proportion to the increases observed in basal metabolic rate (BMR).

An interesting contrast appeared between the two cycle phases; the follicular phase women appeared to lose most of their weight as lean tissue whereas the luteal phase women lost most of their weight as fat.

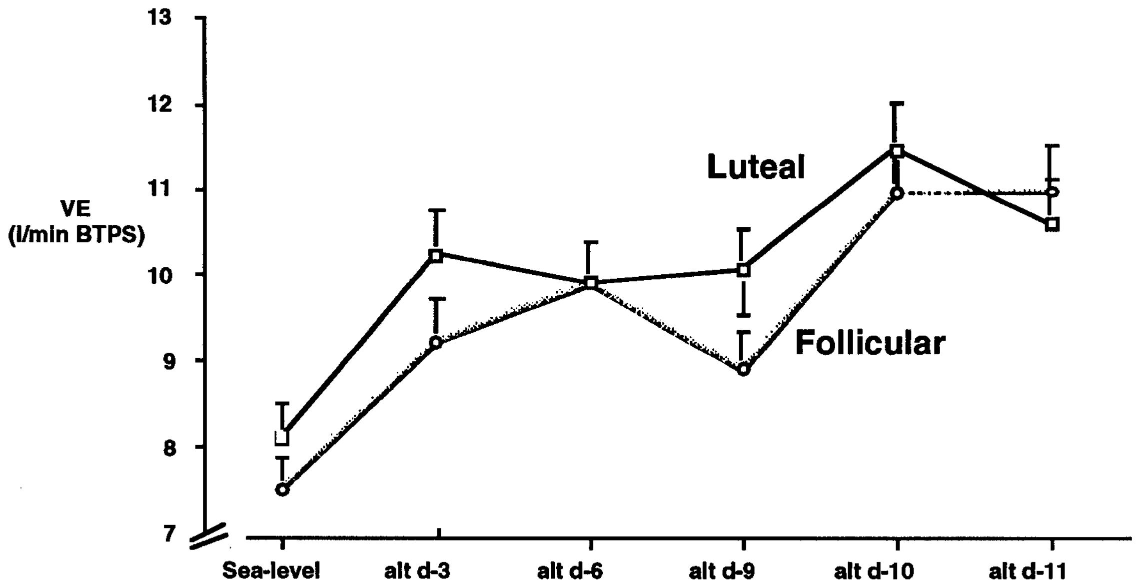


Measurements of total blood volume and total body water have not yet been analyzed. A crude indication of changes in blood volume can be gained from the measurements of hematocrit or hemoglobin concentration shown below. A rise in hemoglobin occurred in both the follicular and luteal phase women, indicating a probable contraction of plasma volume but the rise in hemoglobin appeared to be greater in the follicular than the luteal phase. This suggested that the contraction of plasma volume was greater in the follicular than the luteal phase and is consistent with evidence from previous studies indicating an expansion of plasma volume in the luteal phase of the menstrual cycle. However definitive assessment of the

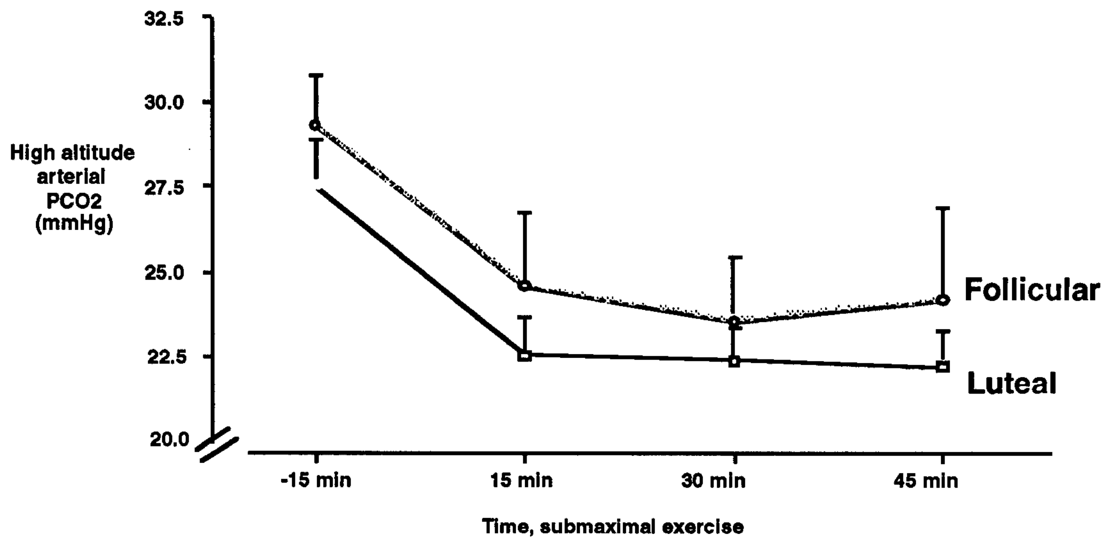
plasma volume changes awaits completion of the blood volume and total body water analyses.



Resting ventilation increased with altitude below but the increase tended to be higher in the luteal than in the follicular phase women.



Arterial O2 saturation did not differ (data not shown). During exercise, the higher levels of effective ventilation appeared to be maintained in the luteal phase women as indicated by lower arterial PCO2 values, as shown below.



The overall pattern of symptoms in the women volunteer test subjects conforms to the pattern of symptoms seen previously in male volunteers studied at the Pikes Pike research facility. Specifically, the scores on both symptoms questionnaires were generally highest on the morning of the second day after ascent and diminished rapidly to sea-level values by the fifth or sixth day. The mean scores were significantly increased over sea-level scores on days 1-3 of altitude exposure. There were no statistically significant differences in mean scores between menstrual cycle phases.

CONCLUSIONS

Very ambitious studies, constituting the first of their kind, have been completed. These studies will provide a complete and well-controlled assessment of the influence of menstrual cycle phase on parameter of oxygen transport both at sea level and at high altitude.

The logistical and scientific scheduling of these studies represented a prodigious effort. Their successful completion reflects very favorably on all the investigative teams involved. THE USARIEM staff was unflagging in their dedication to this project. They helped in the provisioning of equipment and of the Pikes Peak facility, the conduct of tests, and carried out a considerable portion of the studies listed above; namely those in the areas of ventilation and ventilatory control, endurance performance and symptoms of altitude illness. The California team under the leadership of Dr. Gail Butterfield recruited, retained the active cooperation of the study volunteers, and carried out the metabolic testing described above. This involved not only a complex series of measurements during rest and exercise but also the calculation and maintenance of a complete and balanced diet. Extensive fluid volume tests were also carried out by this team. The Colorado team

carried out most of the hematological tests, including the blood volume measurements and collaborated with investigators form the University of Texas to measure cardiac output during exercise. The coordination of study testing, data entry, as well as the placement of arterial and most venous lines was also handled by the Colorado group. It was truly a prodigious, team effort.

The scientific findings to date from the study are exciting. The major observations appear to support the primary study hypotheses but a large amount of additional data needs to be analyzed before such a claim can be made with certainly. To date, the principal findings appear to be that women acclimatizing in the lutes compared to the follicular phases:

- demonstrate weight loss primarily from fat (rather than lean tissue)
- have a lower hemoglobin
- breathe more during rest and exercise
- and tend to have higher arterial PO2 and arterial O2 saturation during exercise.

Thus acclimatization during the luteal phase appears to be, as hypothesized associated with greater effective alveolar ventilation, less plasma volume contraction, and greater fat loss. The extent to which these differences reflect differences in ventilation control, alterations in volume regulatory hormones, sympathetic activity or differences in substrate utilization is currently under study.

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Note: (*) indicates publication from associated laboratories.

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Appendix A. Sea level admission #1 schedule. Each "x" designates a day on which the measurements were made.

SEA LEVEL (F or L)						ADMISSION 1						
Study Day	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Follicular phase	m	m	m	m	m							
Luteal phase	lh+1	ov										
Control diet	x	x	x	x	x	x	x	x	x	x	x	x
Nights in unit						x	x	x	x	x	x	
Body weight	x		x		x	x	x	x	x	x	x	x
Nitrogen balance							x	x	x			
Urine collection		x			x		x	x	x	x	x	
Fecal collection							x	x	x			
BMR							x	x	x			
Pregnancy test			x									
VO2 peak					x							
Substrate utilization										x		
Blood gases/Arterial BP										x		
Meal Tolerance test									x			
Cardiac output, acetylene												
Resting Ve,PetCO2,SaO2,VC	x						x					
HVR,HCVR	x						x					
HR monitoring											x	x
BP monitoring											x	
Catechols-blood			x							x		x
Catechols-urinary		x			x		x	x	x	x	x	
Blood volume												x
Total body water			x									x
Doubly labeled water			x									
Erythropoietin, retics												x
Hgb,hct			x									x
Coag factors												x
Volume regulatory hormones												x
Serum Ov hormones			x							x		x
AMS SX (ESQ & LL)	x		x				x	x	x	x	x	x
Endurance studies	x					x			x			

Appendix B. Sea level admission #2 schedule. Each "x" designates a day on which the measurements were made.

SEA LEVEL (F or L)					**ADMISSION 2**							
Study Day	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Follicular phase	m	m	m	m	m							
Luteal phase	lh+1	ov										
Control diet					x	x	x	x	x	x	x	
Nights in unit									x	x	x	
Body weight					x			x	x	x		
Nitrogen balance												
Urine collection		x			x		x	x	x	x	x	
Fecal collection												
BMR												
Pregnancy test					x							
VO2 peak					x							
Substrate utilization										x		
Blood gases/Arterial BP										x		
Meal Tolerance test									x			
Cardiac output, acetylene										x		
Resting Ve,PetCO2,SaO2,VC	x						x					
HVR,HCVR	x						x					
HR monitoring											x	x
BP monitoring											x	
Catechols-blood	x									x		x
Catechols-urinary		x			x		x	x	x	x	x	
Blood volume												x
Total body water												x
Doubly labeled water												
Erythropoietin, retics												x
Hgb,hct			x									x
Coag factors												x
Volume regulatory hormones												x
Serum Ov hormones	x									x		x
AMS SX (ESQ & LL)	x							x	x	x	x	x
Endurance studies	x				x				x			

Appendix C. Sea level admission #3 schedule. Each "x" designates a day on which the measurements were made.

SEA LEVEL (F or L)						**ADMISSION 3**						
Study day	**1**	**2**	**3**	**3**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Follicular phase	m	m	m	m	m							
Luteal phase	lh+1	ov										
Control diet						x	x	x	x	x		
Nights in unit									x	x		
Body weight									x	x		
Nitrogen balance												
Urine collection												
Fecal collection												
BMR												
Pregnancy test									x			
VO2 peak							x					
Substrate utilization										x		
Blood gases/arterial BP										x		
Meal Tolerance test												
Cardiac Output/acetylene												
Resting Ve,PetCO2,SaO2,VC												
HVR,HCVR												
HR monitoring												
BP Monitoring												
Catechols-blood										x		
Catechols-urinary												
Blood volume												
Total body water												
Doubly labeled water												
Erythropoietin, retics												
Hgb,hct												
Coag factors												
Volume regulatory hormones												
Serum Ov hormones												
AMS SX (ESQ & LL)												
Endurance studies												

Appendix D. High altitude admission #4 schedule. Each "x" designates a day on which the measurements were made.

HIGH ALTITUDE (ADMISSION 4)	Altitude/phase day													
	0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*1*
travel		x											x	:
Follicular events	m	m	m	m	m									
Luteal events	lh	ov												
Protocol diet	x	x	x	x	x	x	x	x	x	x	x	x		
Body weight			x	x	x	x	x	x	x	x	x	x		
Urine collection			x	x	x	x	x	x	x	x	x	x	x	
BMR			x	x	x	x	x	x	x	x	x	x		
Pregnancy test	x											x		
VO2 peak						x								
Substrate utilization											x			
Blood gases/Arterial BP											x			
Cardiac output exercise trial					x						x			
Resting Ve		x	x	x		x		x				x		
HVR,HCVR			x			x		x				x		
HR monitoring			x	x								x	x	
BP monitoring			x	x								x	x	
Catechols-blood				x							x	x		
Catechols-urinary				x	x	x	x	x	x	x	x	x	x	
Meal Tolerance test										x				
Total body water				x								x		
Blood volume				x								x		
Erythropoietin, retics				x			x					x		
Hgb,hct				x			x			x	x	x		
Coag factors												x		
Volume regulatory hormones				x								x		
Serum Ov hormones				x			x			x	x	x		
Endurance studies			x				x					x		
AMS SX (ESQ & LL)	x	x	x	x	x	x	x	x	x	x	x	x		
Lean body mass (DEXA)		x											x	

DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
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REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 3 Mar 00

MEMORANDUM FOR Administrator, Defense Technical Information Center, ATTN: DTIC-OCA, 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical report written for Grant DAMD17-95-C-5110. Request the limited distribution statement for Accession Document Number **ADB218321**, be changed to **"Approved for public release; distribution unlimited."** This report should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Virginia Miller at DSN 343-7327 or by email at virginia.miller@det.amedd.army.mil.

FOR THE COMMANDER:

Phylis M. Rinehart

PHYLIS M. RINEHART
Deputy Chief of Staff for
Information Management